

## SEARCH REQUEST FORM

RECEIVED

Scientific and Technical Information Center

FEB 25 2005

Requester's Full Name: Sabrina Ong Examiner #: 7414 Date: 2/26/05  
 Art Unit: 3716 Phone Number 202-22 Serial Number: 012791331  
 Mail Box and Bldg/Room Location: 2 Results Format Preferred (circle): PAPER DISK E-MAIL  
4C70 - Ram - 4A45 MEJ

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: A GOSTON et al.  
 Inventors (please provide full names): Anti-Angiogenic agents

Earliest Priority Filing Date: 2/8/2001

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for the compds of  
 formula 1.  
 Please not a proviso in all the last  
 line of cl 1.

Please see attached Sheet

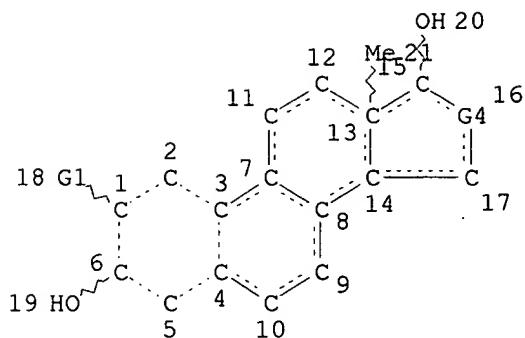
Thank you

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN <u>327.91</u>
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr. Link
Date Completed: <u>3/7</u>	Litigation	Lexis/Nexis
Searcher Prep / Review Time: <u>20</u>	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: <u>20</u>	Other	Other (specify)

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L1

STR



N~N~N  
@22 23 24

C≡C~G2  
@25 26 27

Ak @

CH≡CH~G2  
@28 29 30

Ak~CH≡CH2  
@31 32 33

Ak~Cb~CH≡CH2  
@34 35 36 37

Cb~Ak~CH≡CH2  
@38 39 40 41

C≡CH  
@42 43

Ak~G3  
@44 45

Ak~Cb~G3  
@46 47 48

Cb~Ak~G3  
@49 50 51

Ak~Cb  
@53 54

Cb~Ak  
@55 56

CH~G5  
@57 58

G5~C~G5  
59 @60 61

Cy @62

Page 1-A

52

Page 1-B

VAR G1=22/25/28/31/34/38/42/44/46/49

VAR G2=52/53/55

VAR G3=OH/NH2/CL/BR/I/F/CF3

VAR G4=57/60

VAR G5=AK/62

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Qazi 09/779,331

03/07/2005

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DEFAULT ECLEVEL IS LIMITED

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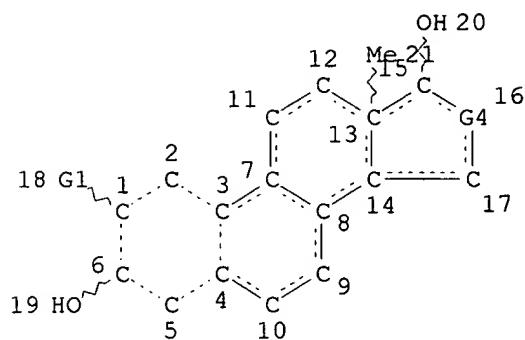
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L1

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N~N~N  
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C≡C~G2  
@25 26 27

Ak @

CH≡CH~G2  
@28 29 30

Ak~CH≡CH2  
@31 32 33

Ak~Cb~CH≡CH2  
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C≡CH  
@42 43

Ak~G3  
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Ak~Cb~G3  
@46 47 48

Cb~Ak~G3  
@49 50 51

Ak~Cb  
@53 54

Cb~Ak  
@55 56

CH~G5  
@57 58

G5~C~G5  
59 @60 61

Cy @62

Page 1-A

52

Page 1-B

VAR G1=22/25/28/31/34/38/42/44/46/49

VAR G2=52/53/55

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VAR G4=57/60

VAR G5=AK/62

#### NODE ATTRIBUTES:

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DEFAULT MLEVEL IS ATOM

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Qazi 09/779, 331

03/07/2005

GGCAT IS UNS AT 35  
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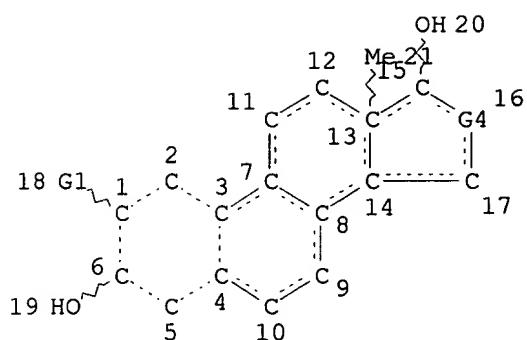
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STEREO\_ATTRIBUTES: NONE  
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L1

STR



N~N~N  
@22 23 24

C≡C~G2  
@25 26 27

Ak @

CH≡CH~G2  
@28 29 30

Ak~CH≡CH2  
@31 32 33

Ak~Cb~CH≡CH2  
@34 35 36 37

Cb~Ak~CH≡CH2  
@38 39 40 41

C≡CH  
@42 43

Ak~G3  
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Ak~Cb~G3  
@46 47 48

Cb~Ak~G3  
@49 50 51

Ak~Cb  
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Cb~Ak  
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CH~G5  
@57 58

G5~C~G5  
59 @60 61

Cy @62

Page 1-A

52

Page 1-B

VAR G1=22/25/28/31/34/38/42/44/46/49

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VAR G5=AK/62

#### NODE ATTRIBUTES:

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DEFAULT MLEVEL IS ATOM

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GGCAT IS UNS AT 35  
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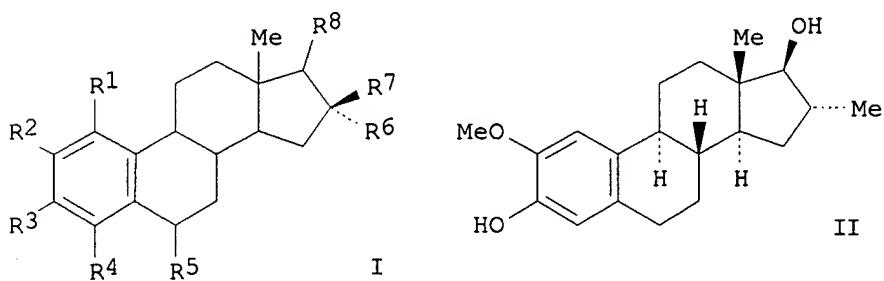
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L7 ANSWER 1 OF 4 MARPAT COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 137:279370 MARPAT  
 TITLE: Preparation of 2-methoxyestradiol derivatives as  
 antiangiogenic agents  
 INVENTOR(S): Agoston, Gregory E.; Pribluda, Victor; Treston,  
 Anthony M.; Green, Shawn J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 15 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

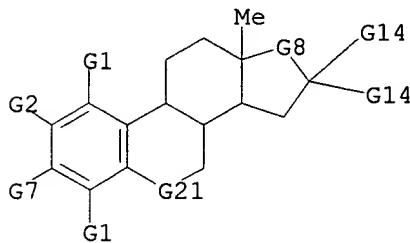
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US 2002147183	A1	20021010	US 2001-779331	20010208
PRIORITY APPLN. INFO.:			US 2001-779331	20010208
OTHER SOURCE(S):		CASREACT 137:279370		

GI



AB Derivs. of 2-methoxyestradiol of formula I [R1, R4 = H, halo, CN, alkyl, OH, CH<sub>2</sub>OH, NH<sub>2</sub>, etc.; R2 = N<sub>3</sub>, CN, alkynyl, alkenyl, alkoxy, etc.; R3 = H, OH, hydroxyalkyl, etc.; R5 = H, oxo, OH, NOH, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, etc.; R8 = OH, oxo, NOH, etc.] are prepared for the treatment of mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol, and had IC<sub>50</sub> of <0.5 μM against MDA-MB-231 human breast carcinoma cells.

## MSTR 1



G2 = N<sub>3</sub>  
G7 = OH  
G8 = 53

HC—G13  
53

G13 = OH  
G14 = Et  
G21 = 144

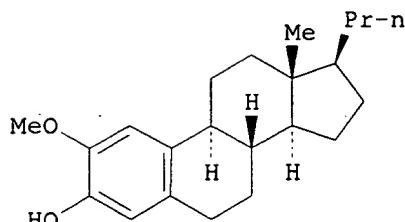
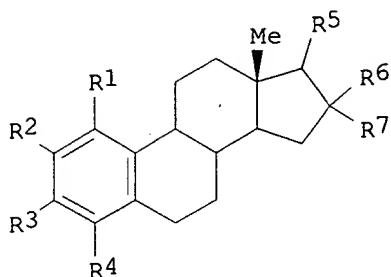
HC—G22  
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MPL: claim 1

L7 ANSWER 2 OF 4 MARPAT COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 137:47357 MARPAT  
 TITLE: Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents  
 INVENTOR(S): Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony M.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

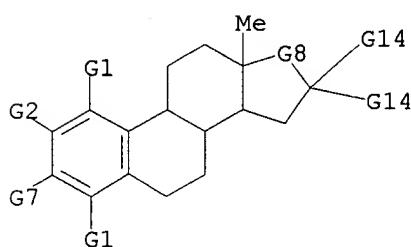
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US 2002082433	A1	20020627	US 2001-939208	20010824
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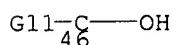


AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH<sub>2</sub>, etc.; R2 = N<sub>3</sub>, CN, OMe, alkenyl, alkynyl, alkoxy, NH<sub>2</sub>, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC<sub>50</sub> of II against MDA-MB-231 breast tumor cells was 51.31 μM.

## MSTR 1



G2 = N<sub>3</sub>  
 G7 = OH  
 G8 = 46



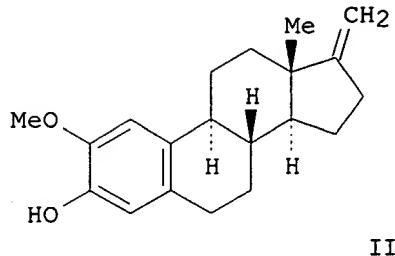
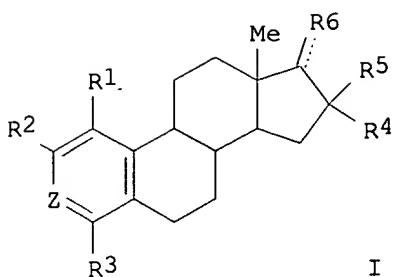
G14 = Et  
 MPL: claim 1

NTE: additional double bond formation also claimed

L7 ANSWER 3 OF 4 MARPAT COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 137:6309 MARPAT  
 TITLE: Preparation of 2-methoxyestradiol analogs as antiangiogenic agents  
 INVENTOR(S): Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony  
 PATENT ASSIGNEE(S): Entremed, Inc., USA  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

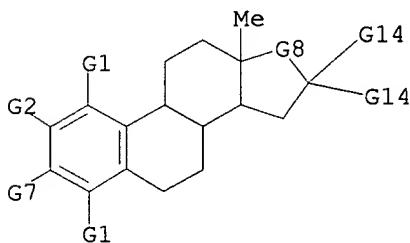
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AU 2001088386	A5	20020603	AU 2001-88386	20010824
EP 1343803	A2	20030917	EP 2001-968112	20010824
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JP 2004537499	T2	20041216	JP 2002-544452	20010824
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			US 2001-278250P	20010323
			US 2001-933894	20010821
			WO 2001-US26490	20010824

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AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH<sub>2</sub>OH, NH<sub>2</sub>, alkylamino; R2 = N<sub>3</sub>, CN, C.tpbond.CR, C=CHR, C.tpbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC<sub>50</sub> 0.24±0 and 0.19±0.19 resp.

**MSTR 1**



G2 = N<sub>3</sub>  
G7 = OH  
G8 = 46

G11—C<sub>46</sub>—OH

G14 = Et  
MPL: claim 1  
NTE: additional double bond formation also claimed

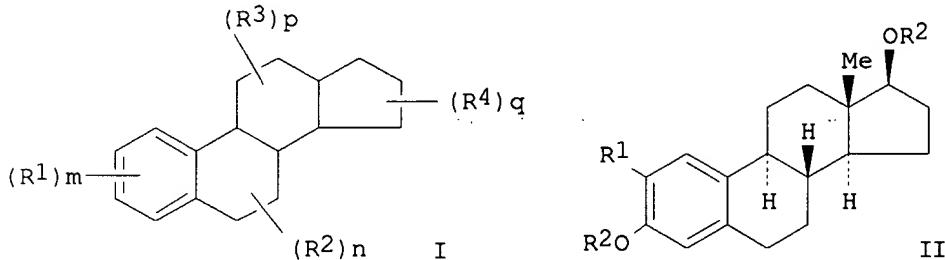
L7 ANSWER 4 OF 4 MARPAT COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 134:295993 MARPAT  
TITLE: Estradiol conjugates and their therapeutic applications  
INVENTOR(S): Stewart, Alastair George; McAllister, David James; Collis, Maree Patricia; Robertson, Alan Duncan

PATENT ASSIGNEE(S): University of Melbourne, Australia  
 SOURCE: PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
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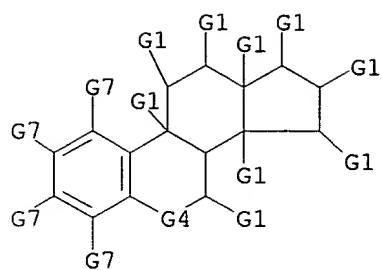
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WO 2001027132	A1	20010419	WO 2000-AU1244	20001013
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AB The invention discloses the preparation of conjugated prodrug of estradiol compound I ( $R_1-R_4 = H, OH, \text{halo, alkyl, alkenyl, alkynyl, cycloalkyl, amino, aryl, keto, hydrazone, oximino, carbohydrate, peptide, etc.}$ ;  $m,n,p,q = 0-3$ ), a pharmaceutically acceptable salt or in vivo hydrolyzable ester, amide carbonate or carbamate thereof, in the treatment of conditions associated with enhanced angiogenesis or accelerated cell division, such as cancer, and inflammatory conditions such as asthma and rheumatoid arthritis and hyperproliferative skin disorders including psoriasis. Thus, II [ $R_1 = OMe$ ,  $R_2 = H$  (III)] was prepared via multi-step reaction sequence starting from  $\beta$ -estradiol II ( $R_1-R_2 = H$ ). In human airway fibroblasts thrombin-stimulated increases in cell number were reduced to  $12 \pm 8\%$  of the control response by III.

MSTR 1



G1 = OH / alkylcarbonyl<(1-5)> / Me  
G4 = 33



G7 = OH / acyl  
MPL: claim 10  
NTE: or derivatives, pharmaceutically acceptable salts, or in vivo hydrolyzable esters, amides, carbonates, or carbamates  
NTE: substitution is restricted  
NTE: also incorporates claim 32, formulas IV, V, and VI

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT